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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,579	05/29/2001	Toshiki Taya	9558-003-27	3666

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EXAMINER	
EINSMANN, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/13/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/865,579	TAYA ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1-4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8* is/are rejected.

7)☒ Claim(s) *5,7 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in Paper No. 12 is acknowledged. The traversal is on the ground(s) that there is no undue burden on the Examiner because any search conducted by the examiner for the process defined by claims 5-8 of the present invention will necessarily encompass a search for the oligonucleotides of claims 1-4. However, this is not persuasive. The separate classification of groups I and II is *prima facie* evidence that the examination of these inventions would place an undue burden on the examiner. Furthermore, the searches required to examine the instantly claimed methods and the instantly claimed probes would be different, requiring a search of different classes, different electronic databases and the use of different key words in such a search. Furthermore, it is noted that the oligonucleotides recited in claims 1-4 are not coextensive with those recited in claims 5-8. Also, the include more than those used in the methods of claims 5-8 and thus, the search of the two sets of claims, even with regard to the polynucleotides is not coextensive. As such, the restriction requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings filed 5/29/01 are approved for examination.

Claim Objections

3. Claim 5 is objected to because it contains a plurality of method steps but not indentations to separate the steps. MPEP 608.01(m) states "Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation, 37 CFR 1.75(i)."

4. Claims 6 and 7 are objected to because they are not proper dependent claims. They do not include all of the limitations of the parent claim from which they depend. Claim 5 requires that one of SEQ ID NO: 18, 22, or 25 is used as a first primer, while claim 6 requires that only a portion of these is used. Thus the scope of claim 6 is broader than the scope of claim 5. Likewise, claim 5 requires that one of SEQ ID NO: 19, 20, 21, 23 or 24 is used as a second primer, but claim 7 requires that only a portion of one of these is used. Thus, the scope of claim 7 is broader than the scope of claim 5 from which it depends.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. Amendment of the claims to clarify active process steps will help to overcome this rejection. Some particular problems in the claims are addressed herein:

Claims 5-8 are indefinite over the recitation "a specific sequence of a RNA derived from mecA gene" because it is not clear what it means for a specific sequence to be "derived from" a mecA gene. That is, it is not clear is this means that the specific sequence is a subsequence of a mecA gene or if it has some other undefined meaning.

Claims 5-8 are indefinite over the recitation "MRSA" because this is an arbitrary abbreviation whose meaning is not defined in the claims.

In claim 5, the phrase "the RNA polymerase promoter" in lines 8-9 lacks proper antecedent basis because the claim does not previously refer to an RNA polymerase promoter.

Claims 5-8 are indefinite because it is not clear which recitations in the claim are positive process steps. For example, the claim recites "forming a double-stranded DNA that includes a promoter sequence allowing transcription of said RNA sequence" but it is not clear if a step of transcribing said RNA sequence is required in the method as an active process step, or if this language is included merely to modify the double-stranded DNA.

Claims 5-8 are further indefinite because the preamble of the claims recites "a detection method employing a RNA amplification process" but the method does not appear to include a detection step. Thus, the relationship between the preamble and the recited method is unclear because it is not clear if applicant intends to claim a detection method or a method for DNA production, as is recited in the claims.

Claims 5-8 are indefinite over the recitation "said double-stranded DNA produces a RNA transcription product" because it is not clear how a double stranded DNA would produce an RNA transcription product, as it is not an enzyme or a process itself, it is in fact a DNA molecule. The recitation "said RNA transcription product is subsequently used as the template for the single-stranded DNA production" for the same reason.

Further, the phrase "the single stranded DNA production" lacks proper antecedent basis in the claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bekkaoui *et al.* (US 6136533) in view of Ryffel *et al.* (Gene, 94 (1999) 137-138).

Bekkaoui *et al.* teach a detection method employing an RNA amplification process which comprises the steps of:

forming a cDNA with a RNA-dependent DNA polymerase using a specific sequence of a RNA present in a sample as a template, with a first primer having a sequence homologous to said specific sequence and a second primer having a sequence complementary to said specific sequence, wherein either the first or second primer has a sequence having an RNA polymerase promoter added at its 5'-region, there by producing an RNA-DNA double strand (Col. 13, lines 25-34);

digesting the RNA of said RNA-DNA double strand with Ribonuclease H to form a single stranded DNA (Col. 13, lines 34-36);

forming a double stranded DNA that includes a promoter sequence allowing transcription of said RNA sequence or a RNA comprising a sequence complementary to said RNA sequence with a DNA-dependent DNA polymerase using said single-stranded DNA as a template, said double-stranded DNA produces a RNA transcription product in the presence of RNA polymerase, and said RNA transcription product is subsequently used as the template for the single stranded DNA production with said RNA-dependent DNA polymerase (Col. 13, lines 36-40).

Bekkaoui *et al.* also teach methods wherein the mecA gene is used as a target for the detection of the presence of methicillin resistant Staphylococcus aureus (Col. 33-35). Bekkaoui *et al.* teach a probe useful for such detection, namely their SEQ ID NO: 4. This sequence taught by Bekkaoui *et al.* overlaps with instant SEQ ID NO: 20 and SEQ ID NO: 21. Particularly, instant SEQ ID NO: 20 falls entirely within the region of the mecA gene that the probe taught by Bekkaoui *et al.* teach. Bekkaoui *et al.* further provide guidance as to how to select probes useful for the methods disclosed in their patent (Col. 6). Bekkaoui *et al.* do not exemplify the RNA amplification process for the detection of the mecA gene, nor do they teach primers that consist of instant SEQ ID NO: 18, 19, 20, 21, 22, 23, 24, or 25.

Ryffel *et al.* provide the full length sequence of the mecA gene isolated from three different methicillin resistant Staphylococci. Ryffel *et al.* specifically point out the regions where the sequence of the mecA gene is identical between the three versions of the gene, and the regions that differ between them. Each of nucleic acid primers SEQ ID NO: 18-25 disclosed herein is contained within the sequence taught by Ryffel *et al.* For example, instant SEQ ID NO: 18 is identical to nucleotides 749-776 of the sequence taught by Ryffel et al, and instant SEQ ID

NO: 20 is identical to the complement of nucleotides 1082-1102 of the sequence taught by Ryffel *et al.*

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the RNA amplification method taught by Bekkaoui *et al.* for the detection of the mecA gene in a sample. The ordinary practitioner would have been so motivated by the teachings of Bekkaoui *et al.* of the RNA amplification method and the exemplification of the mecA gene as a marker of MRSA in a sample. The use of the method taught by Bekkaoui *et al.* for the detection of the mecA gene in a sample would necessarily have required the selection of primers from within the mecA gene. In light of the teachings of Ryffel *et al.*, who provide the full length sequence of the mecA gene from different MRSA, it would have been prima facie obvious to one of ordinary skill in the art to have selected any of the primers disclosed as SEQ ID NO: 18-25. The ordinary practitioner would have been motivated to select these primers because they are each within a region of the mecA gene that is conserved among the different versions of the mecA gene. Selection of primers in such regions would increase the likelihood of detection of each of the three versions of the mecA gene. Thus, in light of the teachings of the prior art, the instant invention is *prima facie* obvious.

10. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bekkaoui *et al.* in view of Ryffel *et al.* as applied to claims 5, 6, and 7 above, and further in view of Ishiguro *et al.* (Nucleic Acids Research, 1996, Vol. 24, No. 24, pages 4992-4997).

The teachings of Bekkaoui *et al.* in view of Ryffel *et al.* are applied to claim 8 as they are applied in the previous rejection. Bekkaoui *et al.* in view of Ryffel *et al.* do not provide a method which includes an oligonucleotide probe labeled with an intercalator fluorescent dye

wherein the probe is complementary to the RNA transcription product and wherein the binding of the probe to said RNA transcription product results in a change of the fluorescent property relative to that of a situation where a complex formation is absent, then measuring the fluorescence intensity of the reaction solution.

Ishiguro *et al.* teach methods wherein a probe labeled with an intercalator fluorescent dye is included in an *in vitro* transcription application in order to provide an easy and specific homogeneous method to detect a nucleic acid sequence (p. 4992). Ishiguro *et al.* teach that "The present success of the applicability of the probe to real-time monitoring of the in vitro transcription showed that YO-linked DNA probe can be a powerful tool with which to construct a new methodology to study the dynamics of gene expression, and also to provide a more practical way of detecting and quantifying a target sequence in a clinical specimen specifically in a homogeneous format (p. 4997)." Thus, in light of the teachings of Ishiguro *et al.*, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included an oligonucleotide probe labeled with an intercalator fluorescent dye wherein the probe is complementary to the RNA transcription product in the method taught by Bekkaoui *et al.* in view of Ryffel *et al.* The ordinary practitioner would have been motivated to include such a probe in order to provide a practical way of detecting and quantifying target sequence in a clinical specimen in a homogeneous format, as is taught by Ishiguro *et al.*

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824.

The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1634

February 6, 2003

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